	Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	259415	(growth adj hormone) or gh	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 14:57			0
2	BRS	L2	3655	replacement adj therapy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 14:56			0
3	BRS	L3	112	1 same 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 14:56			0
4	BRS	L4	14	growth adj hormone adj replacement adj therapy	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 14:59			0
5	BRS	L5	1344	maintenance adj dose	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:00			0
6	BRS	L6	2279	initial adj dose	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:00			0
7	BRS	L7	0	3 same 5 same 6	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:00			0
8	BRS	L8	0	3 same 5	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:01			0
9	BRS	L9	20344	microsphere	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:01			0
10	BRS	L10	0	3 same 9	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:01			0
11	BRS	L11	13	3 same individual$3	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:06			0
12	BRS	L13	106	foster adj michael.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:15			0
13	BRS	L14	2	3 and 13	USPAT; US-PGPUB; EPO; JPO; DERWENT	2002/11/29 15:15			0

> d his

(FILE 'HOME' ENTERED AT 15:19:58 ON 29 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
15:20:28 ON 29 NOV 2002

L1 209152 S GROWTH HORMONE
L3 73580 S REPLACEMENT THERAPY
L5 2712 S L1 (P) L3
L6 13208 S (INITIAL DOSE)
L7 9172 S (MAINTENANCE DOSE)
L8 0 S L5 (P) L6 (P) L7
L9 77643 S MICROSPHERE
L10 0 S L5 (P) L9
L11 215 S L5 (P) INDIVIDUAL?
L12 66 S L11 (P) DOSE
L13 27 S L5 (P) (L6 OR L7)
L14 10 DUPLICATE REMOVE L13 (17 DUPLICATES REMOVED)
L15 24 DUPLICATE REMOVE L12 (42 DUPLICATES REMOVED)
L16 19 S L15 NOT L14

=> log y

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FILE 'HOME' ENTERED AT 15:19:58 ON 29 NOV 2002

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COST IN U.S. DOLLARS                                  SINCE FILE      TOTAL
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FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:20:28 ON 29 NOV 2002

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FILE 'AGRICOLA' ENTERED AT 15:20:28 ON 29 NOV 2002

=> s growth hormone
L1      209152 GROWTH HORMONE

=> s replcement therapy
L2           2 REPLCEMENT THERAPY

=> s replacement therapy
L3       73580 REPLACEMENT THERAPY

=> s l1 (p) l2
L4           0 L1 (P) L2

=> s l1 (p) l3
L5        2712 L1 (P) L3

=> s (initial dose)
L6       13208 (INITIAL DOSE)

=> s (maintenance dose)
L7        9172 (MAINTENANCE DOSE)

=> s l5 (p) l6 (p) l7
L8           0 L5 (P) L6 (P) L7

=> s microsphere
L9       77643 MICROSPHERE

=> s l5 (p) l9
L10          0 L5 (P) L9

=> s l5 (p) individual?
L11        215 L5 (P) INDIVIDUAL?

=> s l11 (p) dose
L12         66 L11 (P) DOSE

=> d his

     (FILE 'HOME' ENTERED AT 15:19:58 ON 29 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:20:28 ON 29 NOV 2002
L1       209152 S GROWTH HORMONE
L2            2 S REPLCEMENT THERAPY
L3        73580 S REPLACEMENT THERAPY
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L4            0 S L1 (P) L2
L5         2712 S L1 (P) L3
L6        13208 S (INITIAL DOSE)
L7         9172 S (MAINTENANCE DOSE)
L8            0 S L5 (P) L6 (P) L7
L9        77643 S MICROSPHERE
L10           0 S L5 (P) L9
L11         215 S L5 (P) INDIVIDUAL?
L12          66 S L11 (P) DOSE

=> s l5 (p) (l6 or l7)
L13          27 L5 (P) (L6 OR L7)

=> duplicate remove l13
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L13
L14           10 DUPLICATE REMOVE L13 (17 DUPLICATES REMOVED)

=> d l14 1-10 ibib abs

L14  ANSWER 1 OF 10     MEDLINE                                DUPLICATE 1
ACCESSION NUMBER:   2001674990     MEDLINE
DOCUMENT NUMBER:    21577789   PubMed ID: 11720895
TITLE:              Systemic ghrelin levels in subjects with growth hormone
                    deficiency are not modified by one year of growth hormone
                    replacement therapy.
AUTHOR:             Janssen J A; van der Toorn F M; Hofland L J; van Koetsveld
                    P; Broglio F; Ghigo E; Lamberts S W; Jan van der Lely A
CORPORATE SOURCE:   Department of Internal Medicine, University of Turin,
                    Italy.. janssen@inw3.azr.nl
SOURCE:             EUROPEAN JOURNAL OF ENDOCRINOLOGY, (2001 Dec) 145 (6)
                    711-6.
                    Journal code: 9423848. ISSN: 0804-4643.
PUB. COUNTRY:       England: United Kingdom
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
ENTRY MONTH:        200201
ENTRY DATE:         Entered STN: 20011127
                    Last Updated on STN: 20020125
                    Entered Medline: 20020111
AB   OBJECTIVE: Ghrelin stimulates   ***growth***     ***hormone***   (GH)
     secretion both in vivo and in vitro. Ghrelin is mainly produced in and
     released from the stomach but it is probably also produced in the
     hypothalamic arcuate nucleus. Whether pituitary GH release is under the
     control of ghrelin from the stomach and/or from the arcuate nucleus is not
     known. Moreover, no data on the feedback of GH on systemic ghrelin
     concentrations are available. It has recently been suggested that ghrelin
     may induce obesity. DESIGN: In this study, we addressed the following two
     questions: a) are circulating ghrelin levels increased in human GH
     deficiency (GHD), and b) does GH treatment modify ghrelin levels in human
     GHD? METHODS: The study group consisted of 23 patients with GHD. Eighteen
     had developed adult-onset GHD and five had developed GHD in their
     childhood (childhood-onset GHD). Ghrelin was measured with a commercially
     available radioimmunoassay. All measurements were performed twice, first
     at baseline, before the start of GH   ***replacement***     ***therapy***
     , and then again after one year of therapy. GH doses were adjusted every 3
     months, targeting serum total IGF-I levels within the normal gender- and
     age-related reference values for the healthy population.
       ***Maintenance***     ***doses***   were continued once the target serum
     total IGF-I levels were reached. RESULTS: The sum of skinfolds and body
     water increased significantly, body fat mass and percentage body fat
     decreased significantly and body mass index and waist-hip ratio were not
     significantly changed by one year of GH   ***replacement***
       ***therapy***  .Before the start of GH   ***replacement***
       ***therapy***  , mean value and range for fasting ghrelin in the studied
     GHD subjects tended to be lower in comparison with healthy subjects in the
     control group although the difference did not reach significance (GHD
     ghrelin mean 67.8 pmol/l, range 37.6-116.3 pmol/l; control mean 83.8
     pmol/l, range 35.4-132 pmol/l; P=0.11).One year of GH   ***replacement***
       ***therapy***   did not modify circulating ghrelin levels (ghrelin before
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GH therapy: 67.8 pmol/l, range 37.6-116.3 pmol/l; after GH therapy: 65.3 pmol/l, range 35.8-112.6; [illegible]0.56). CONCLUSIONS: We did not [illegible]serve elevated ghrelin levels in adult GHD subjects and GH ***replacement*** ***therapy*** did not modify circulating ghrelin levels, despite significant decreases in body fat mass and percentage body fat. It is conceivable that the lack of ghrelin modifications after long-term GH therapy was due to the reduction of adiposity and insulin on one hand, and increased GH secretion on the other. However, it is still possible that systemic ghrelin is involved in the development of obesity, both in normal and GHD subjects.

L14 ANSWER 2 OF 10 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001610300 MEDLINE
DOCUMENT NUMBER: 21541381 PubMed ID: 11684878
TITLE: Body composition and quality of life as markers of the efficacy of growth hormone replacement therapy in adults.
AUTHOR: Svensson J; Johannsson G; Bengtsson B A
CORPORATE SOURCE: Research Centre for Endocrinology and Metabolism, Sahlgrenska University Hospital, Goteborg, Sweden.. Johan.Svensson@medic.gu.se
SOURCE: HORMONE RESEARCH, (2001) 55 Suppl 2 55-60. Ref: 43
Journal code: 0366126. ISSN: 0301-0163.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 20011102
Last Updated on STN: 20020125
Entered Medline: 20020107
AB ***Growth*** ***hormone*** (GH) ***replacement*** ***therapy*** in GH-deficient adults should be initiated with a low dose, independent of body weight or body surface area. Measurements of serum insulin-like growth factor I (IGF-I) concentrations, as well as clinical examinations aimed at detecting signs of fluid excess, are important as safety markers to avoid overtreatment with GH. At present, there is no optimal marker for the long-term efficacy of GH ***replacement*** ***therapy*** . The long-term ***maintenance*** ***dose*** of GH should, therefore, be titrated in each individual based on the clinical response, with the aim of normalizing body hydration, other measurements of body composition, quality of life and well-being, and biochemical indices such as serum IGF-I concentration.
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L14 ANSWER 3 OF 10 MEDLINE
ACCESSION NUMBER: 2001084938 MEDLINE
DOCUMENT NUMBER: 20557181 PubMed ID: 11105553
TITLE: [Effects of growth hormone replacement therapy in adults with severe growth hormone deficiency].
Novekedesi hormonnal torteno hormonpotlo kezeles hatasai sulyos novekedesi hormonhianyos felnottekben.
COMMENT: Comment in: Orv Hetil. 2000 Oct 29;141(44):2381-2
AUTHOR: Hubina E; Kovacs L; Szabolcs I; Rimanoczy E; Ferencz A; Czirjak S; Toth M; Szucs N; Racz K; Goth M
SOURCE: ORVOSI HETILAP, (2000 Oct 29) 141 (44) 2375-9.
Journal code: 0376412. ISSN: 0030-6002.
PUB. COUNTRY: Hungary
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hungarian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010118
AB The aim of the study was to analyse the effects of GH ***replacement*** ***therapy*** (1 year duration) on body composition, carbohydrate metabolism, thyroid hormone metabolism and bone mineral density in 8 adults with ***growth*** ***hormone*** deficiency (5 women, 3 men; mean age 40 years). Mean ***maintenance*** ***dose*** of GH was 1.5 IU/day-1.76 IU/day for women and 1.07 IU/day for men,

respectively--determined according to individual patient requirements. Serum insulin-like growth factor-I standard deviation score increased from -5.4 to 0.0 ($p < 0.001$). There was a significant negative relationship between serum insulin-like growth factor-I standard deviation score at the start of therapy and the increase in this score ($r = -0.85$; $p < 0.05$). The waist:hip ratio decreased after 12 months by 0.039 ($p < 0.05$). The glycosylated hemoglobin increased (4.43 +/- 0.56% vs. 5.86 +/- 0.27; $p < 0.05$), and a negative correlation of the baseline glycosylated hemoglobin to the glycosylated hemoglobin increase was found ($r = -0.88$; $p < 0.01$). Both the free triiodothyronine and free triiodothyronine:free thyroxine ratio increased (3.09 +/- 0.22 vs. 4.17 +/- 0.40; $p < 0.05$, and 0.234 +/- 0.02 vs. 0.324 +/- 0.04; $p < 0.01$), and a positive relationship was observed between this ratio at the start of therapy and the increase in the ratio ($r = 0.76$, $p < 0.05$). The bone mineral density of lumbar spine and femoral neck expressed as z-score increased (-1.18 +/- 0.56 vs. -0.75 +/- 0.48; $p < 0.01$ and -0.06 +/- 0.60 vs. 0.43 +/- 0.43; $p < 0.05$), while the bone mineral density of forearm was unchanged. CONCLUSIONS: ***Growth*** ***hormone*** replacement leads to a decrease in visceral fat, modulates the thyroid hormone levels by increasing peripheral conversion of thyroxine to triiodothyronine and probably is a physiological regulator of peripheral thyroxine metabolism, slightly deteriorates the carbohydrate metabolism, and results in an increase of bone mineral density of lumbar spine and femoral neck.

L14 ANSWER 4 OF 10 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 1999398244 MEDLINE
DOCUMENT NUMBER: 99398244 PubMed ID: 10468941
TITLE: GH replacement in 1034 growth hormone deficient hypopituitary adults: demographic and clinical characteristics, dosing and safety.
AUTHOR: Abs R; Bengtsson B A; Hernberg-Stahl E; Monson J P; Tauber J P; Wilton P; Wuster C
CORPORATE SOURCE: Department of Endocrinology, University Hospital, Antwerp, Belgium.
SOURCE: CLINICAL ENDOCRINOLOGY, (1999 Jun) 50 (6) 703-13.
Journal code: 0346653. ISSN: 0300-0664.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 19991101
Entered Medline: 19991021

AB OBJECTIVE: Long-term experience of ***growth*** ***hormone*** (GH) ***replacement*** ***therapy*** in a large population of hypopituitary adults with GH deficiency (GHD) is limited, and safety surveillance is clearly essential. KIMS, the Pharmacia & Upjohn International Metabolic Database, is a long-term, open, outcomes research programme of hypopituitary adult patients with GHD who are treated in a conventional clinical setting. PATIENTS: The present analysis encompasses data from 1034 hypopituitary adult GHD patients treated with GH for a total of 818 patient years. RESULTS: Prior to GH therapy, the KIMS patient population exhibited an increased prevalence of obesity, diabetes mellitus (in females) and hyperlipidaemia, compared with normal populations described in published studies. Quality of life, assessed using a disease-specific questionnaire (QoL-AGHDA), was also reduced in KIMS patients. The ***maintenance*** ***dose*** of GH was significantly higher in patients who were receiving GH prior to enrolment into KIMS (non-naive patients) compared with patients who commenced GH at the time of enrolment (naive patients). In addition, dose of GH correlated significantly with body weight in the former group of patients. Analysis of serum levels of IGF-I indicated that overtreatment with GH was markedly more common in non-naive than in naive patients. The frequency of adverse events in KIMS patients was no higher than that reported in patients receiving placebo in previous clinical trials. Recurrence of pituitary or CNS tumours was reported in six patients, a rate consistent with data from control series. Three deaths were reported, none of which was obviously associated with GH treatment. CONCLUSIONS: Our data, drawn from a large population of hypopituitary adults treated with GH for a total of more than 800 patient years, confirm previous reports that untreated GHD in hypopituitary adults is associated with a number of important clinical

problems. In addition, the results suggest that there has been a shift in recent years from determination of GH dose on the basis of body weight to dose titration of individual patients, and indicate that the latter technique has important advantages. The data provide further evidence that GH ***replacement*** ***therapy*** is well-tolerated in adults. However, it is possible that some adverse events may not become evident over the time scale covered by the present analysis, and continued surveillance therefore remains mandatory.

L14 ANSWER 5 OF 10 MEDLINE
ACCESSION NUMBER: 1999293930 MEDLINE
DOCUMENT NUMBER: 99293930 PubMed ID: 10365596
TITLE: [The beneficial effects of growth hormone replacement therapy on elderly men].
Korzystny wplyw uzupelniania niedoboru hormonu wzrostu u starszych mezczyzn.
AUTHOR: Kozakowski J; Adamkiewicz M; Krassowski J; Zgliczynski S
CORPORATE SOURCE: Kliniki Endokrynologii Centrum Medycznego Ksztalcenia Podyplomowego, Szpital Bielanski w Warszawie.
SOURCE: POLSKI MERKURIUSZ LEKARSKI, (1999 Mar) 6 (33) 131-4.
Journal code: 9705469. ISSN: 1426-9686.
PUB. COUNTRY: Poland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Polish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990707
AB The relationship of ***growth*** ***hormone*** (GH) to the ageing process is currently subject of considerably interest. The study was designed to investigate the effects of ***replacement*** ***therapy*** with ***growth*** ***hormone*** on quality of life, serum lipids and body composition (fat free mass and fat mass) in elderly men. MATERIAL: 18 healthy men 60.0 +/- 2.4 (x +/- SEM) years of age. Their body weight was 78.6 +/- 4.6 kg and body mass index (BMI) was 26.5 +/- 1.4 kg/m2. Diagnosis of GH deficiency was based on serum insulin-like growth factor-1 (IGF-1) levels below 200 micrograms/L (138.1 +/- 9.2), abolished GH nocturnal surge and diminished glucagon-stimulated GH secretion compared to reference group of young men (16.2 +/- 1.8 to 30.6 +/- 4.7 micrograms/L/hour; p < 0.02 and 10.8 +/- 1.0 to 44.1 +/- 15.3 micrograms/L/hour; p < 0.02, respectively). Reference group comprised nine men 27.5 +/- 1.3 years of age with body weight 76.3 +/- 2.2 kg and BMI 23.1 +/- 0.6 kg/m2. The subjects received recombinant, human GH daily subcutaneously during 12 months in dose adjusted to maintain optimal (280-350 micrograms/L) serum IGF-1 level. The ***initial*** ***dose*** was 0.125 IU/kg b.w./week. Before, and after 6 and 12 months of therapy clinical and laboratory exams, including serum GH, IGF-1 and lipids levels, and body composition using two methods were obtained. Quality of life was assessed by modified Beck's questionnaire. 12-months ***replacement*** ***therapy*** with ***growth*** ***hormone*** in elderly men improved mental status, increased serum IGF-1 level to the young normal men values, from 138.1 +/- 9.2 to 279.4 +/- 26.3 micrograms/L, p < 0.001, reduced serum LDL-cholesterol from 3.67 +/- 0.12 to 3.10 +/- 0.21 mmol/L, p < 0.04 and increased serum HDL and HDL2 levels from 1.20 +/- 0.05 to 1.41 +/- 0.08 mmol/L, p < 0.002 and from 0.19 +/- 0.03 to 0.34 +/- 0.06 mmol/L, p < 0.005, respectively, reduced fat mass (12.8%, p < 003), particularly localised in trunk (14.7%, p < 0.03), and increased fat free mass (2.9%, p < 0.03). GH- ***replacement*** ***therapy*** in elderly men has beneficial effects on quality of life, and may counteract ageing and atherosclerosis progression by serum lipids and body composition improvement.

L14 ANSWER 6 OF 10 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 1999029605 MEDLINE
DOCUMENT NUMBER: 99029605 PubMed ID: 9814468
TITLE: Optimizing growth hormone replacement therapy by dose titration in hypopituitary adults.
AUTHOR: Drake W M; Coyte D; Camacho-Hubner C; Jivanji N M; Kaltsas G; Wood D F; Trainer P J; Grossman A B; Besser G M; Monson J P
CORPORATE SOURCE: Department of Endocrinology, St Bartholomew's and The Royal

London School of Medicine and Dentistry, St Bartholomew's Hospital, [redacted] Kingdom.
SOURCE: JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (1998 Nov) 83 (11) 3913-9.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199811
ENTRY DATE: Entered STN: 19990106
Last Updated on STN: 19990106
Entered Medline: 19981125

AB Although ***growth*** ***hormone*** (GH) ***replacement*** ***therapy*** is increasingly utilized in the management of adult hypopituitary patients, optimum dosing schedules are poorly defined. The use of weight-based or surface area-based dosing may result in overtreatment, and individual variation in susceptibility on the basis of gender and other factors is now being recognized. To optimize GH replacement and to explore further gender differences in susceptibility, we used a dose titration regimen, starting at the initiation of GH ***replacement*** ***therapy*** , in 50 consecutive adult-onset hypopituitary patients, and compared the results with those in 21 patients previously treated using a weight-based regimen. Titrated patients commenced GH 0.8 IU/day subcutaneously (0.4 IU/day if hypertensive or glucose tolerance impaired). Serum insulin-like growth factor I (IGF-I) was measured at 0, 2, 4, 6, 8, 10, and 12 weeks in all patients. Serum IGF binding protein 3 and acid labile subunit were measured at the same time points in 17 patients (8 male, 9 female). Patients were reviewed every 4 weeks and the dose of GH increased, if necessary, to achieve a serum IGF-I level between the median and the upper end of the age-related reference range. There was no significant difference between mean serum IGF-I at 2 and 4 weeks, or between 6 and 8 weeks, indicating that the full effects of a change in dose are evident within 2 weeks of that change. ***Maintenance*** ***doses*** were significantly higher in females than males [1.2 (0.8-2.0) vs. 0.8 (0.4-1.6) IU/day; median (range); P < 0.0001], and the median time to achieve ***maintenance*** ***dose*** was significantly shorter in males [4 (2-12) vs. 9 (2-26) weeks; P < 0.0001]. Median ***maintenance*** ***dose*** was lower overall than in a group of 21 patients initially commenced on GH using a weight-based dosing schedule, with subsequent adjustment of dose during clinical follow-up [1.5 (0.4-3.2) IU/day; P = 0.02]. Reduction in waist measurement and waist to hip ratio at 6 and 12 months was similar in females (P < 0.001) and males (P < 0.01). Well-being improved significantly after 3 months of GH therapy (14.2 +/- 5.9 vs. 7.4 +/- 4.5 SD; P < 0.0001), and there were no gender differences. Adult ***Growth*** ***Hormone*** Deficiency Assessment (AGHDA) scores at 6 months were similar to maintenance scores in patients commenced on weight-based regimens. Measurements of ALS and IGFBP-3 added no useful extra information to IGF-I in managing the dose titration. The practical scheme outlined for dose titration of GH replacement resulted in rapid achievement of lower ***maintenance*** ***doses*** than those achieved using conventional weight-based regimens without loss of efficacy. It was particularly important in female patients who demonstrated decreased overall sensitivity to GH and required higher doses to achieve the same effects as males. This constitutes the first report of a uniform titration regimen based on a defined target range of serum IGF-I in a large patient cohort.

L14 ANSWER 7 OF 10 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999267520 MEDLINE
DOCUMENT NUMBER: 99267520 PubMed ID: 10335039
TITLE: [The effect of growth hormone replacement therapy on markers of bone formation and bone mineral density in elderly men].
Wplyw uzupelniania niedoborow hormonu wzrostu na wskazniki syntezy i gestosc mineralna kosci u starszych mezczyzn.
AUTHOR: Kozakowski J; Papierska L; Krassowski J; Zgliczynski S
CORPORATE SOURCE: Klinika Endokrynologii Centrum Medycznego Ksztalcenia Podyplomowego, Szpital Bielanski w Warszawie.

SOURCE: POLSKIE ARCHIWUM MEDYCYNY WEWNETRZNEJ, (1998 Oct) 100 (4) 306-12.
Journal code: 0401225. ISSN: 0032-3772.
PUB. COUNTRY: Poland
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Polish
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990707

AB OBJECTIVE: Decline in ***growth*** ***hormone*** (GH) secretion and serum levels of insulin-like growth factor-1 (IGF-1) during ageing may be a causal factor in the development of osteopenia. The purpose of this study was to test the effects of GH- ***replacement*** ***therapy*** on bone metabolism and mineral density in healthy men over 40 years old. MATERIAL: 18 healthy men aged 60.2 +/- 2.4 (avg +/- SEM) with mean body weight 78.6 +/- 4.6 kg and body mass index (BMI) 26.5 +/- 1.4 kg/m2. Diagnosis of ***growth*** ***hormone*** deficiency was based on serum IGF-1 levels below 200 micrograms/L (138.1 +/- 9.2), abolished GH nocturnal surge and diminished glucagon-stimulated GH secretion compared to reference group of young men (16.2 +/- 1.8 to 30.6 +/- 4.7 micrograms/L/hour; $p < 0.02$ and 10.8 +/- 1.0 to 44.1 +/- 15.3 micrograms/L/hour; $p < 0.02$ respectively). Nine healthy men aged 27.5 +/- 1.3 were recruited as a control subjects. Their body weight was 76.3 +/- 2.2 kg and BMI 21.3 +/- 0.6 kg/m2. METHODS: The subjects received human, recombinant GH (rhGH) daily subcutaneously during 12 months in dose individually adjusted to maintain optimal (280-350 micrograms/L) serum IGF-1 level. ***Initial*** ***dose*** was 0.125 IU/kg b.w./week. Before and after 6 and 12 months of therapy clinical and laboratory exams, including serum GH, IGF-1, calcium, phosphate, osteocalcin, glucose, insulin levels and alkaline phosphatase (AP) activity were obtained. Lumbar spine and femoral neck bone mineral density (BMD) were measured by dual-energy X-ray absorptiometry. RESULTS: rhGH administration for 12 months led to a significant increase in mean serum IGF-1 levels, from 138.1 +/- 9.2 to 279.4 +/- 26.3 micrograms/L ($p < 0.001$). Mean serum osteocalcin concentration rose from 19.4 +/- 1.7 to 34.4 +/- 4.7 micrograms/L ($p < 0.004$), and serum AP activity changed nearly significantly, from 78.0 +/- 4.8 to 88.1 +/- 7.2 U/L. Lumbar spine and femur neck BMD increased significantly after 12 months, from 1.092 +/- 0.05 to 1.119 +/- 0.06 g/cm2 ($p < 0.05$) and from 0.886 +/- 0.04 to 0.905 +/- 0.04 g/cm2 ($p < 0.05$), respectively. CONCLUSION: ***Growth*** ***hormone*** ***replacement*** ***therapy*** in elderly men may be regarded as a method useful to protect against osteoporosis progression.

L14 ANSWER 8 OF 10 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:74999 BIOSIS
DOCUMENT NUMBER: PREV199800074999
TITLE: Guidelines for optimizing growth hormone replacement therapy in adults.
AUTHOR(S): de Boer, Hans (1); Van Der Veen, Eduard
CORPORATE SOURCE: (1) Spaarne Ziekenhuis Haarlem, PO Box 1644, NL-2003 BR Haarlem Netherlands
SOURCE: Hormone Research (Basel), (Nov., 1997) Vol. 48, No. SUPPL. 5, pp. 21-30.
ISSN: 0301-0163.
DOCUMENT TYPE: Article
LANGUAGE: English

AB To minimize the rate of side-effects, a retrospective analysis of 28 studies of GH replacement therapy in adults indicates that the maintenance dose should usually not exceed 1.0 IU/m2/day (about 1.5-2.0 IU/day) in GHD patients 40-60 years old, or 1.5 IU/m2/day (about 2.5-3.0 IU/day) in GHD patients 20-40 years old. GHD women may tolerate, and in fact may need, higher replacement doses, though this issue requires further investigation. GH treatment should be started at a low dose, i.e. about 1.0 IU/day, and increased gradually, by about 0.5 IU per month, until the target dose is reached. In the absence of side-effects, the GH dose may be either too low, adequate, or too high. Measurement of GH-dependent serum markers provides the most promising approach to detect both GH depletion

and excess, with serum IGF-I concentration the current method of choice. Clinical awareness of symptoms of GH excess remains important, however, particularly in patients with IGF-I levels in the high normal range.

L14 ANSWER 9 OF 10 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97296773 EMBASE
DOCUMENT NUMBER: 1997296773
TITLE: Growth hormone deficiency in adults and growth hormone replacement therapy.
AUTHOR: Irie M.; Hara Y.
CORPORATE SOURCE: M. Irie, Toho University, Research Center, Sumitomo Pharmaceuticals Co., Ltd., Sumitomo, Japan
SOURCE: Japanese Pharmacology and Therapeutics, (1996) 24/10 (195-228).
Refs: 285
ISSN: 0386-3603 CODEN: YACHDS
COUNTRY: Japan
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English; Japanese
AB This review summarizes the current information regarding the clinical aspects of ***growth*** ***hormone*** deficiency (GHD) in adults and the effects of GH replacement in GHD adults. Recent research has confirmed previous clinical suspicion that adults with GHD have impaired physical and psychological performance even in the presence of adequate adrenal, thyroid and gonadal hormone ***replacement*** ***therapy*** . This GHD syndrome is characterised particularly by impaired psychological well-being, abnormal body composition with increased abdominal adiposity, reduced strength and exercise capacity, reduced basal metabolic rate, reduced bone density and an elevation in total and low density lipoprotein cholesterol. The finding of the effect of GH on lipid metabolism may be important in the context of the observed increase in cardiovascular mortality rates of GHD adults. Convincing evidence now exists that GH ***replacement*** ***therapy*** can successfully reverse many of the characteristic physical, psychological and metabolic changes associated with GHD. A number of key clinical trials have demonstrated significant shifts in body composition, with the ratio of lean body mass: fat mass tending towards normal, a concomitant increase in extracellular water, and a small but significant rise in bone mineral content. At the same time, cardiac and renal functions are improved, and exercise capacity is markedly increased. Adverse effects of GH therapy are few and have probably been overstated due to excessive doses used in the initial studies. These can be minimized by starting at a low ***initial*** ***dose*** and increasing gradually while monitoring clinical response and serum insulin-like growth factor-1 values. Since recombinant technology has solved the limitations in GH supply, policies concerning GH ***replacement*** ***therapy*** in man may be reconsidered. The observed beneficial effects of GH treatment are certainly of sufficient magnitude to consider treatment of all adults with the diagnosis of GHD. Increased awareness of the symptoms and signs of this condition, and of the diagnostic process for identifying GHD adults, should do much to promote improvement in this new therapeutic area.

L14 ANSWER 10 OF 10 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 95324418 MEDLINE
DOCUMENT NUMBER: 95324418 PubMed ID: 7601008
TITLE: Growth hormone replacement therapy for growth hormone-deficient adults.
AUTHOR: Powrie J; Weissberger A; Sonksen P
CORPORATE SOURCE: Division of Medicine, United Medical School of Guy's Hospital, London, England.
SOURCE: DRUGS, (1995 May) 49 (5) 656-63. Ref: 48
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199508
ENTRY DATE: Entered STN 19950822
Last Updated on STN: 19950822
Entered Medline: 19950810

AB Recent research has confirmed previous clinical suspicion that adults with pituitary disease and ***growth*** ***hormone*** (GH) deficiency have impaired physical and psychological performance even in the presence of adequate adrenal, thyroid and gonadal hormone ***replacement*** ***therapy*** . This GH deficiency syndrome is characterised particularly by impaired psychological well-being, abnormal body composition with increased abdominal adiposity, reduced strength and exercise capacity, reduced basal metabolic rate, reduced bone density and an elevation in total and low density lipoprotein cholesterol. This latter finding may be important in the context of the observed increase in cardiovascular mortality rates of GH-deficient adults. GH ***replacement*** ***therapy*** administered as a once-daily subcutaneous injection can restore a near normal quality of life to many of these patients, although there is as yet no evidence that this treatment reduces mortality. Adverse effects of GH therapy are few and have probably been overstated due to excessive doses used in the initial studies. These can be minimised by starting at a low ***initial*** ***dose*** and increasing gradually while monitoring clinical response and serum insulin-like growth factor-1 values. All adults with GH deficiency should now be considered for GH ***replacement*** ***therapy*** .

=> d his

(FILE 'HOME' ENTERED AT 15:19:58 ON 29 NOV 2002)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 15:20:28 ON 29 NOV 2002

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L1      209152 S GROWTH HORMONE
L2           2 S REPLCEMENT THERAPY
L3       73580 S REPLACEMENT THERAPY
L4           0 S L1 (P) L2
L5        2712 S L1 (P) L3
L6       13208 S (INITIAL DOSE)
L7        9172 S (MAINTENANCE DOSE)
L8           0 S L5 (P) L6 (P) L7
L9       77643 S MICROSPHERE
L10          0 S L5 (P) L9
L11        215 S L5 (P) INDIVIDUAL?
L12         66 S L11 (P) DOSE
L13         27 S L5 (P) (L6 OR L7)
L14         10 DUPLICATE REMOVE L13 (17 DUPLICATES REMOVED)
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=> duplicate remove l12
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L12
L15 24 DUPLICATE REMOVE L12 (42 DUPLICATES REMOVED)

=> s l15 not l14
L16 19 L15 NOT L14

=> d l16 1-19 ibib abs

L16 ANSWER 1 OF 19 MEDLINE
ACCESSION NUMBER: 2002651941 IN-PROCESS
DOCUMENT NUMBER: 22298825 PubMed ID: 12413201
TITLE: Optimizing delivery of therapeutics: percutaneous technologies.
AUTHOR: Henzl M R
CORPORATE SOURCE: The Department of Gynecology and Obstetrics, Stanford University School of Medicine, California, USA.. mhenzl@aol.com
SOURCE: BRATISLAVSKE LEKARSKE LISTY, (2002) 103 (4-5) 144-51. Journal code: 0065324. ISSN: 0006-9248.
PUB. COUNTRY: Slovakia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English

FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021105
Last Updated on STN: 20021105

AB The purpose of this communications is to 1) demonstrate the potential of percutaneous drug-delivery on the example of female reproductive steroids, 2) point out the differences between transdermal and conventional drug dosing, and 3) outline new technologies and innovations that are looming on the horizon, specifically in the area of pain control. Transdermal delivery systems are of two basic types. The first ones employ principles of passive diffusion, and they are used for hormonal ***replacement*** ***therapy*** (HRT) and contraception. Patches for HRT, designed to release estradiol (E2) only, require a simultaneous dosing with oral progestogens. Patches employing both E2 and a progestogen release the combination either continuously or sequentially. In the latter method, estrogen-only patches are applied for 14 days, followed by a 14-day application of patches releasing both hormones. Both methods successfully cope with symptoms and signs of menopause, including bone loss. Contraceptive transdermal patches deliver ethinylestradiol in combination with the progestogen norelgestromin. This system provides high contraceptive protection with predictable withdrawal bleeding and without major adverse events and weight changes. Hormones delivered by the skin avoid first-pass liver metabolism. Other advantages include rapid onset and termination of action, self-administration, and attainment of therapeutic hormone levels with low daily ***doses*** . A disadvantage is the variable intra- and inter- ***individual*** percutaneous absorption. In some patients, patches can cause skin irritation. Active systems deliver therapeutics across intact skin non-invasively by means of an electric potential (electrotransport). A system consisting of tooth-like titanium microprojections that penetrate only the keratinized epidermis facilitates painless and needle-free transport of complex molecules to the capillaries of the dermis. Other devices use low frequency ultrasound. These systems enable precise dosage, delivery of large molecules, such as ***growth*** ***hormone*** and vaccines, and dosing of analgesics "on demand". Novel transdermal technologies are profoundly changing the current methods of pain management. (Fig. 6, Ref. 47.).

L16 ANSWER 2 OF 19 MEDLINE
ACCESSION NUMBER: 2002637623 IN-PROCESS
DOCUMENT NUMBER: 22283688 PubMed ID: 12396230
TITLE: Long-term growth hormone replacement therapy in hypopituitary adults.
AUTHOR: Verhelst Johan; Abs Roger
CORPORATE SOURCE: Departments of Endocrinology, Middelheim Hospital and University Hospital, Antwerp, Belgium.
SOURCE: DRUGS, (2002) 62 (16) 2399-412.
Journal code: 7600076. ISSN: 0012-6667.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021026
Last Updated on STN: 20021026

AB ***Growth*** ***hormone*** deficiency (GHD) in the adult has now been fully recognised as a clinical entity characterised by abnormal body composition, osteopenia, impaired quality of life, cardiac dysfunction and an adverse lipid profile. While short-term studies of GH replacement have demonstrated irrefutably a favourable effect on all if not most features of GHD, data on long-term administration spanning more than 2 years are still scarce. Experience of GH replacement up to 5 to 10 years indicate that the beneficial effects on body composition, predominantly a decrease in body fat and an increase in lean mass, is maintained during treatment. Long-term GH therapy also increases muscle strength and exercise performance. All data, with one exception, are consistent with a significant increase in bone mass during prolonged GH therapy. The most distinct effect on bone was observed in the worst affected ***individuals*** and in males. Improvement in quality of life is documented shortly after initiation of GH replacement and is maintained during long-term studies. This may explain the reduction in days of sick leave seen during GH therapy. The beneficial effect on cardiovascular risk factors is sustained over a prolonged period of time, revealing a reduction in intima wall thickness, and an improvement in serum lipid

levels and clotting parameters. The increase in lipoprotein(a) levels with GH therapy in some studies may be disturbing, but difficulties in measuring this parameter and inconsistencies between the different studies makes it difficult to estimate its real impact. No data are yet available to show that GH replacement will normalise or even improve mortality rate and fracture rate. Adverse events associated with GH ***replacement*** ***therapy*** are mainly secondary to fluid retention as a result of excess ***dose*** administration. This can be adequately prevented by monitoring GH replacement according to serum insulin-like growth factor (IGF)-I levels. From what is currently known, GH replacement does not increase the prevalence of diabetes mellitus, and does not induce new neoplasms or recurrence of the primary brain tumour; however, longer follow-up studies are needed to provide definitive answers. In conclusion, it appears not only that long-term GH ***replacement*** ***therapy*** in adults with GHD is a procedure that can be safely used, but that GH replacement should be considered as a possible life-long therapy in order to maintain its benefits.

L16 ANSWER 3 OF 19 MEDLINE
ACCESSION NUMBER: 2001232355 MEDLINE
DOCUMENT NUMBER: 21066659 PubMed ID: 11146379
TITLE: Bone markers and bone mineral density during growth hormone treatment in children with growth hormone deficiency.
AUTHOR: Cowell C T; Woodhead H J; Brody J
CORPORATE SOURCE: Robert Vines Growth Research Centre, Ray Williams Institute of Endocrinology Diabetes and Metabolism, The Children's Hospital at Westmead, Parramatta, NSW, Australia.. chrisc@nch.edu.au
SOURCE: HORMONE RESEARCH, (2000) 54 Suppl 1 44-51. Ref: 26
Journal code: 0366126. ISSN: 0301-0163.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517
Entered Medline: 20010503

AB ***Growth*** ***hormone*** (GH) has a positive impact on muscle mass, growth and bone formation. It is known to interact with the bone-forming unit, with well-documented increases in markers of bone formation and bone resorption within weeks of the start of GH therapy. These changes relate significantly to short-term growth rate, but it is not evident that they predict long-term response to GH therapy. The consequences of GH deficiency (GHD) and GH ***replacement*** ***therapy*** on bone mineral density (BMD) have been difficult to interpret in children because of the dependency of areal BMD on height and weight. Some studies have tried to overcome this problem by calculating volumetric BMD, but results are conflicting. The attainment of a normal peak bone mass in an ***individual*** is considered important for the future prevention of osteoporosis. From the limited data available, it appears difficult to normalize bone mass totally in GH-deficient ***individuals*** , despite GH treatment for long periods. Studies to date examining the interaction between GH and bone have included only small numbers of ***individuals*** , making it difficult to interpret the study findings. It is hoped that these issues can be clarified in future research by the direct measurement of bone density (using quantitative computer tomography). Mineralization is only one facet of bone strength, however; other important components (e.g. bone structure and geometry) should be addressed in future paediatric studies. Future studies could also address the importance of the degree of GHD in childhood; how GH ***dose*** and insulin-like growth factor-I levels achieved during therapy relate to the final outcome; whether or not the continuation of GH therapy after the attainment of final height may further enhance bone mass; whether the timing and ***dose*** of other treatments (e.g. sex hormone ***replacement*** ***therapy***) are critical to the outcome; and whether GHD in childhood is associated with an increased risk of fracture.
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L16 ANSWER 4 OF 19 MEDLINE
ACCESSION NUMBER: 2001196897 MEDLINE
DOCUMENT NUMBER: 21144878 PubMed ID: 11249503
TITLE: Growth hormone: current and future therapeutic applications.
AUTHOR: Murray R D; Shalet S M
CORPORATE SOURCE: Department of Endocrinology, Christie Hospital, NHS Trust, Wilmslow Road, Manchester, M20 4BX, UK.
SOURCE: Expert Opin Pharmacother, (2000 Jul) 1 (5) 975-90. Ref: 97
Journal code: 100897346. ISSN: 1465-6566.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010410
Last Updated on STN: 20010410
Entered Medline: 20010405

AB The increased availability of ***growth*** ***hormone*** (GH) in the mid-1980s, as a result of advances in recombinant DNA techniques, has allowed research into the use of this hormone at physiological dosage, as ***replacement*** ***therapy*** for adults with GH deficiency (GHD) and at pharmacological dosages as a possible therapeutic agent, for a number of disease states. GHD adults have increased body fat and reduced muscle mass and consequently, reduced strength and exercise tolerance. In addition, they are osteopenic, have unfavourable cardiac risk factors and impaired quality of life. In these ***individuals*** , replacing GH reverses these anomalies, although it may not alter the reduced insulin-sensitivity. A proportion of adults with GHD perceive a dramatic improvement in their well-being, energy levels and mood following replacement. GH has protein and osteoanabolic, lipolytic and antinatriuretic properties. GH has been considered for the therapeutic treatment of frailty associated with ageing, osteoporosis, morbid obesity, cardiac failure, major thermal injury and various acute and chronic catabolic conditions. Initial small, uncontrolled studies for many of these clinical problems suggested a beneficial effect of GH, although, later placebo-controlled studies have not observed such dramatic effects. Furthermore, with a recent publication demonstrating an approximate 2-fold increase in mortality in critically ill patients receiving large ***doses*** of GH, the use of GH should remain in the realms of ***replacement*** ***therapy*** and research, until there are significant advances in our understanding.

L16 ANSWER 5 OF 19 MEDLINE
ACCESSION NUMBER: 2001119915 MEDLINE
DOCUMENT NUMBER: 20537491 PubMed ID: 11086656
TITLE: The importance of growth hormone replacement therapy for bone mass in young adults with growth hormone deficiency.
AUTHOR: Attie K M
CORPORATE SOURCE: Department of Medical Affairs, Genentech, Inc., South San Francisco, CA 94080, USA.. kma@gene.com
SOURCE: JOURNAL OF PEDIATRIC ENDOCRINOLOGY AND METABOLISM, (2000 Sep) 13 Suppl 2 1011-21. Ref: 68
Journal code: 9508900.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010215

AB ***Growth*** ***hormone*** (GH) plays an important role in longitudinal bone growth in childhood, accrual of peak bone mass, and bone preservation in adults. GH deficiency (GHD) is associated with reduced bone turnover and decreased bone mineral density (BMD), especially in patients with childhood-onset GHD. GH ***replacement*** ***therapy*** stimulates bone remodeling and causes an initial decrease

in BMD due to bone resorption and expansion of the remodeling space. This is followed by increased bone formation and a significant increase in BMD that continues with prolonged GH therapy. The effect appears to be ***dose*** -dependent. GH ***dose*** should be ***individualized*** based on factors such as age, oral estrogen therapy, and IGF-I levels. Young GH-deficient adults with low BMD measurements by dual-energy X-ray (DEXA) scan should be considered for GH ***replacement*** ***therapy*** to reduce future fracture risk.

L16 ANSWER 6 OF 19 MEDLINE
ACCESSION NUMBER: 2001095891 MEDLINE
DOCUMENT NUMBER: 20437565 PubMed ID: 10984262
TITLE: Effects of growth hormone on bone and muscle.
AUTHOR: Lissett C A; Shalet S M
CORPORATE SOURCE: Department of Endocrinology, Christie Hospital, Withington, Manchester, UK.. mmassey@picr.man.ac.uk
SOURCE: GROWTH HORMONE AND IGF RESEARCH, (2000 Apr) 10 Suppl B S95-101. Ref: 43
Journal code: 9814320. ISSN: 1096-6374.
PUB. COUNTRY: SCOTLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB The decade since the initial availability of recombinant ***growth*** ***hormone*** (GH) has seen an increase in our understanding of the effects of GH on muscle and bone. Adult GH deficiency (GHD) is associated with osteopenia, the severity of which is related to three factors: the timing, age of onset and severity of GHD. Epidemiological data suggest that this osteopenia is associated with an increased risk of fracture. The impact of GH ***replacement*** ***therapy*** on bone mineral density (BMD) appears to be related to a large number of interrelated factors, including the ***dose*** and duration of therapy, timing of onset of GHD, skeletal site, degree of osteopenia at baseline, and age and gender of the patient. Overall, the effect of GH replacement on BMD in the majority of patients is beneficial. As yet, however, no data are available that demonstrate a reduction in fracture rate following GH therapy. In comparison with normal ***individuals*** , GH-deficient ***individuals*** have reduced lean body mass and muscle strength, both of which increase within 12 months of GH therapy. Therefore, the effects of GH replacement on muscle and bone in GH-deficient ***individuals*** are significant and beneficial, although the longer-term effects of GH replacement in terms of reducing the number of fractures and prevention of frailty in old age are not yet established. The effects of GH on bone and muscle in GH-replete ***individuals*** have been studied less fully. While GH therapy modulates markers of bone resorption and formation, its effects in patients with idiopathic osteoporosis are disappointing, with oestrogen therapy or bisphosphonates proving to be more effective in post-menopausal women. To date, however, there have been no GH treatment trials of adequate duration (longer than 18 months), and it remains possible that longer-term trials may demonstrate more profound effects. The effects of GH therapy on muscle have been examined in normal elderly ***individuals*** . Generally, the ***doses*** used have been supraphysiological and associated with an unacceptable incidence of side-effects. GH therapy has resulted in an increase in lean body mass, but functional ability and strength have not improved in the majority of studies. Thus, clear-cut beneficial effects of GH on muscle and bone in GH-replete ***individuals*** have not been demonstrated. It seems unlikely that normal elderly ***individuals*** will benefit significantly from GH therapy, but frail ***individuals*** or those with musculoskeletal or neuromuscular pathology are potential candidates for study.

L16 ANSWER 7 OF 19 MEDLINE
ACCESSION NUMBER: 2000182937 MEDLINE
DOCUMENT NUMBER: 20182937 PubMed ID: 10720018
TITLE: Treatment of growth hormone deficiency in adults.

AUTHOR: Bengtsson B A; Johannsson G; Shalet S M; Simpson H; Sonken P H
CORPORATE SOURCE: Research Center for Endocrinology and Metabolism, Sahlgrenska University Hospital, Goteborg, Sweden.
SOURCE: JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, (2000 Mar) 85 (3) 933-42. Ref: 59
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000407
Last Updated on STN: 20000407
Entered Medline: 20000330

AB In analogy with other hormonal ***replacement*** ***therapy*** GH treatment should be commenced with a low starting ***dose*** , independent of body weight or body surface area. Hormonal replacement should mimic the normal physiology to minimize the risk of side effects in the life-long replacement of adults. We should, therefore, consider ***individual*** responsiveness and also be aware of the difference between pattern of GH under normal condition and during s.c. administration. The safety and monitoring of GH ***replacement*** ***therapy*** in adults have been addressed in the ***Growth*** ***Hormone*** Research Society Consensus Guidelines for Diagnosis and Treatment of Adults with GH Deficiency from the Port Stephens Workshop, April 1997. Besides finding better and more accurate biochemical markers for choosing correct GH replacement ***dose*** , future research should address the long-term benefits and safety with GH replacement in adults, with special emphasize on incipient risks in terms of cardiovascular disease and of neoplasia, in particular.

L16 ANSWER 8 OF 19 MEDLINE
ACCESSION NUMBER: 2000062749 MEDLINE
DOCUMENT NUMBER: 20062749 PubMed ID: 10592459
TITLE: Determination of insulin-like growth factor-I in the monitoring of growth hormone treatment with respect to efficacy of treatment and side effects: should potential risks of cardiovascular disease and cancer be considered?.
AUTHOR: Juul A
CORPORATE SOURCE: Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark.. ajuul@post4.tele.dk
SOURCE: HORMONE RESEARCH, (1999) 51 Suppl 3 141-8. Ref: 100
Journal code: 0366126. ISSN: 0301-0163.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000421
Last Updated on STN: 20000421
Entered Medline: 20000411

AB Insulin-like growth factor (IGF)-I has proven to be important in the diagnosis of childhood-onset ***growth*** ***hormone*** (GH) deficiency (GHD). However, the variability of IGF-I should be taken into account before it can be used in a clinical setting. GH ***replacement*** ***therapy*** in GHD patients increases IGF-I into the normal range, although there is a large variation. Excessively high (supranormal) GH-induced IGF-I levels are associated with increased prevalence of side effects in adults with GHD. Consequently, at most centres, GH ***doses*** are titrated according to IGF-I levels in GHD adults. Whether or not this should also be done in children has not been established. Due to the known variability of IGF-I, ***individual*** changes in IGF-I must exceed approximately 35% to be sufficiently significant to warrant a ***dose*** adjustment. Novel epidemiological studies have suggested that higher IGF-I levels are associated with an increased risk of prostate, breast and colorectal cancer compared with lower IGF-I levels in otherwise healthy subjects. Consequently, life-time

exposure to IGF-I should be considered in all patients treated with GH, and IGF-I should preferably be kept within normal age-related ranges in children as well as in adults. Copyright Copyright 1999 S. Karger AG, Basel

L16 ANSWER 9 OF 19 MEDLINE
ACCESSION NUMBER: 1999202287 MEDLINE
DOCUMENT NUMBER: 99202287 PubMed ID: 10102059
TITLE: Effect of growth hormone (GH) during puberty in GH-deficient children: preliminary results from an ongoing randomized trial with different dose regimens.
AUTHOR: Albertsson Wikland K; Alm F; Aronsson S; Gustafsson J; Hagenas L; Hager A; Ivarsson S; Kristrom B; Marcus C; Moell C; Nilsson K O; Ritzen M; Tuvemo T; Westgren U; Westphal O; Aman J
CORPORATE SOURCE: Department of Pediatrics, Sahlgrenska University Hospital/East, Goteborg, Sweden.
SOURCE: ACTA PAEDIATRICA. SUPPLEMENT, (1999 Feb) 88 (428) 80-4. Journal code: 9315043. ISSN: 0803-5326.
PUB. COUNTRY: Norway
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990527

AB This paper reports results from an ongoing, randomized, multicentre national trial. The aim is to elucidate whether a ***dose*** of ***growth*** ***hormone*** (GH) of 0.2 IU/kg (0.07 mg/kg), given either as once-daily or twice-daily injections during puberty, is more effective than a once-daily ***dose*** of 0.1 IU/kg/day (0.03 mg/kg/day) in improving final height in children with GH deficiency (GHD). The twice-daily regimen comes closer to the spontaneous GH secretion pattern in puberty. Ninety-two children with GHD who had been receiving GH therapy for at least 1 year, and with spontaneous puberty or who were prepubertal and due to be started on ***replacement*** ***therapy*** to induce puberty, were randomly assigned to receive GH as follows: group A, 0.1 IU/kg/day (0.03 mg/kg/day), administered once daily; group B, 0.2 IU/kg/day (0.07 mg/kg/day), administered once daily; and group C, 0.2 IU/kg/day (0.07 mg/kg/day), divided into two equal injections given at 12-hour intervals. Pubertal height gain was 0.7, 0.7 and 1.3 SDS for groups A, B and C, respectively. The gain in height during puberty was thus most marked in group C. Mean final height, when corrected for parental height, was between 0 and 1 SDS in all treatment groups. All but seven children reached a final height within +/- 2 SD of the general population. There was a wide range of final heights in all three treatment groups. This variation in response suggests the need to ***individualize*** treatment in order to achieve an appropriate final height for most ***individuals*** .

L16 ANSWER 10 OF 19 MEDLINE
ACCESSION NUMBER: 97032173 MEDLINE
DOCUMENT NUMBER: 97032173 PubMed ID: 8878069
TITLE: Superoxide anion release from neutrophils in growth hormone deficient adults before and after replacement therapy with recombinant human growth hormone.
AUTHOR: Reinisch N; Schratzberger P; Finkenstedt G; Kahler C M; Wiedermann C J
CORPORATE SOURCE: Department of Internal Medicine, University of Innsbruck, Austria.
SOURCE: NAUNYN-SCHMIEDEBERGS ARCHIVES OF PHARMACOLOGY, (1996 Aug-Sep) 354 (3) 369-73. Journal code: 0326264. ISSN: 0028-1298.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970305
Last Updated on STN: 19970305
Entered Medline: 19970218

AB The observations that ***growth*** ***hormone*** primes neutrophils and stimulates various activities of monocytes suggested that it plays a role in the regulation of leukocyte biology. The in vivo reduction of ***growth*** ***hormone*** levels may be responsible for to the functional impairment of leukocytes observed in ***growth*** ***hormone*** deficient children. Whether leukocyte function is impaired in ***growth*** ***hormone*** deficient adults is not known as yet. We therefore studied superoxide anion release from neutrophils and chemotaxis of monocytes in 15 patients with adult-onset ***growth*** ***hormone*** deficiency before and after a period of 6 months of ***replacement*** ***therapy*** with recombinant human ***growth*** ***hormone*** . Analyses were performed by comparing functions of the leukocytes from these patients with those from age and sex-matched healthy control subjects. Before ***growth*** ***hormone*** treatment, patients received appropriate ***replacement*** ***therapy*** with thyroid, adrenal and gonadal hormones. The ***dose*** of recombinant human ***growth*** ***hormone*** was 0.25-0.5 U/kg/week (0.013-0.026 mg/kg/day) throughout the whole period of ***replacement*** ***therapy*** . In ***growth*** ***hormone*** deficient subjects, formylpeptide-triggered release of superoxide anions from neutrophils was significantly suppressed by about 40% before treatment as compared to healthy control subjects. After 6 months of ***replacement*** ***therapy*** , neutrophil superoxide anion release was similar in patients and healthy ***individuals*** . Neither before nor after ***replacement*** ***therapy*** , however, was there a difference in monocyte migration between control and ***growth*** ***hormone*** deficient subjects. These data indicate that neutrophil function is somehow altered in ***growth*** ***hormone*** deficient patients, even when receiving appropriate therapy with thyroid, adrenal and gonadal hormones, but that neutrophil function can be restored to near normalcy by ***growth*** ***hormone*** ***replacement*** ***therapy*** . This would suggest that suppressed neutrophil respiratory burst is due to the deficiency in ***growth*** ***hormone*** .

L16 ANSWER 11 OF 19 MEDLINE
ACCESSION NUMBER: 96159840 MEDLINE
DOCUMENT NUMBER: 96159840 PubMed ID: 8589319
TITLE: The effects of prolonged substitution of recombinant human growth hormone on renal functional reserve in growth hormone-deficient adults.
AUTHOR: Riedl M; Hass M; Oberbauer R; Gisinger J; Luger A; Mayer G
CORPORATE SOURCE: Department of Internal Medicine III, University Hospital of Vienna, Austria.
SOURCE: JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (1995 Nov) 6 (5) 1434-8.
Journal code: 9013836. ISSN: 1046-6673.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199603
ENTRY DATE: Entered STN: 19960404
Last Updated on STN: 19960404
Entered Medline: 19960327

AB Twelve ***growth*** ***hormone*** (GH)-deficient adults with normal renal function were recruited for a 6-month, double-blind, placebo-controlled study on the effects of prolonged recombinant human ***growth*** ***hormone*** (rhGH) substitution therapy on renal functional parameters. RhGH was administered at a ***dose*** 0.125 IU/kg per week sc the first 4 wk and 0.25 IU/kg per week thereafter. At baseline and after 6 months of therapy, GFR and RPF were measured by the use of iothalamate and para- aminohippurate clearance techniques before and after an intravenous infusion of amino acids (AA) to determine the

renal functional reserve capacity (RFRC). At baseline, GFR and RPF were similar in the GH-deficient patients and a group of normal healthy controls (GFR, 117 +/- 10 mL/min; RPF, 567 +/- 57 mL/min, and filtration fraction, 22 +/- 1.6% in the patient group and GFR, 117 +/- 10 mL/min; RPF, 509 +/- 54 mL/min; and filtration fraction, 24 +/- 1.3% in the control group). GFR increased significantly in the control and patient group after AA infusion; the RFRC, however, was significantly larger in healthy ***individuals*** (GFR post-AA infusion, 141 +/- 10 mL in GH-deficient patients and 182 +/- 20 mL/min in controls). Thereafter, six patients received placebo therapy for 6 months and GFR as well as RFRC remained constant (GFR, 107 +/- 9 and 106 +/- 12 mL/min before AA infusion and 132 +/- 14 and 134 +/- 5 mL/min after AA infusion at baseline and after 6 months, respectively). Four patients of the placebo group then continued with rhGH therapy for another 6 months. They and six patients who had rhGH therapy from the beginning form the rhGH treatment study group. During rhGH treatment, plasma insulin-like growth factor activity increased significantly from 93 +/- 17 to 229 +/- 23 ng/mL. Baseline GFR and RPF as well as RFRC were unaltered by the 6 months of rhGH ***replacement*** ***therapy*** (basal GFR, 124 +/- 7 mL/min before and 123 +/- 9 mL/min after 6 months of rhGH therapy; GFR after AA infusion, 145 +/- 9 mL/min at baseline and 144 +/- 8 mL/min after 6 months of therapy). Kidney size as evaluated by ultrasonography was normal at baseline when compared with that in age- and sex-matched controls (10.3 +/- 0.2 versus 9.9 +/- 0.1 cm) and was unchanged after 6 months of therapy (10.3 +/- 0.3 cm). It was concluded from this study that rhGH substitution for 6 months at a ***dose*** of 0.25 IU/kg per week in GH-deficient patients with normal renal function has no adverse functional effects on the kidney.

L16 ANSWER 12 OF 19 MEDLINE
ACCESSION NUMBER: 95237813 MEDLINE
DOCUMENT NUMBER: 95237813 PubMed ID: 7721271
TITLE: Consequences of growth hormone deficiency in adults and the benefits and risks of recombinant human growth hormone treatment. A review paper.
AUTHOR: Rosen T; Johannsson G; Johansson J O; Bengtsson B A
CORPORATE SOURCE: Research Centre for Endocrinology and Metabolism, RCEM, Sahlgrenska University Hospital, Goteborg, Sweden.
SOURCE: HORMONE RESEARCH, (1995) 43 (1-3) 93-9. Ref: 63
Journal code: 0366126. ISSN: 0301-0163.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199505
ENTRY DATE: Entered STN: 19950605
Last Updated on STN: 19950605
Entered Medline: 19950519
AB ***Growth*** ***hormone*** deficiency (GHD) in adults is now recognized as a specific clinical syndrome with characteristic symptoms and signs. Thus, the patients are overweight, have an abnormal body composition (excess body fat and a decrease in the extracellular water volume) and a low bone mineral content compared to normals. Furthermore, the GHD patients have lipid abnormalities, decreased insulin sensitivity and a decreased fibrinolysis. Finally, the 'quality of life' is low in terms of energy and social life. Short- and long-term studies with recombinant human GH (rhGH) treatment have shown normalization of body composition, increase in the lipid pattern and marked improvement of the psychological well-being. The treatment seems safe with no serious side effects reported. In analogy with other hormonal ***replacement*** ***therapies*** , the rhGH ***dose*** should be ***individualized*** .

L16 ANSWER 13 OF 19 MEDLINE
ACCESSION NUMBER: 90038197 MEDLINE
DOCUMENT NUMBER: 90038197 PubMed ID: 2809097
TITLE: Biosynthetic human growth hormone: current status and future questions.
AUTHOR: Thompson R G; Conforti P; Holcombe J
CORPORATE SOURCE: Eli Lilly and Company, Lilly Research Laboratories,

Indianapolis, Indiana 46285.
SOURCE: JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION, 89) 12 (8 Suppl 3) 35-9.
Journal code: 7806594. ISSN: 0391-4097.
PUB. COUNTRY: Italy
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19891220

AB Human ***growth*** ***hormone*** derived from human pituitaries resulted in excellent growth in children with ***growth*** ***hormone*** deficiency but limited supplies in many countries prevented treatment of all children, delayed the onset of therapy, and/or forced the use of ***doses*** that may have been less than optimal. Recent advances in technology allow the production of byosynthetic human ***growth*** ***hormone*** (hGH) by recombinant methods resulting in increased supplies of hormone. More than 200 previously untreated children with ***growth*** ***hormone*** deficiency have been evaluated for two years or longer while receiving biosynthetic natural sequence hGH (somatropin). The mean growth velocity of 3.6 cm/yr prior to therapy increased to 8.8 cm/yr after one year and 7.25 cm/yr in the second year. Growth response was inversely related to age when calculated as cm/yr. This response paralleled the normal decrease in growth velocity as children approach puberty. Children with hGH deficiency who had previously received replacement hGH were enrolled in a double-blind study using either 0.06 or 0.10 mg/kg thrice weekly for 12 months. Growth rate was significantly greater with the higher ***dose*** during the first six months but not during the second six month period. The use of a higher ***dose*** of hGH must be ***individualized*** as not all patients have accelerated growth with the increased ***dose*** and the mean group response is not permanent. Multiple questions remain unanswered after three decades of treating ***growth*** ***hormone*** deficiency. Are the current criteria for diagnosis of ***growth*** ***hormone*** deficiency appropriate? What ***dose*** of hGH is correct? Do children need increases in ***replacement*** ***therapy*** as their height approaches normal?(ABSTRACT TRUNCATED AT 250 WORDS)

L16 ANSWER 14 OF 19 MEDLINE
ACCESSION NUMBER: 86127174 MEDLINE
DOCUMENT NUMBER: 86127174 PubMed ID: 3946325
TITLE: Russell-Silver syndrome and hypopituitarism. Patient report and literature review.
AUTHOR: Cassidy S B; Blonder O; Courtney V W; Ratzan S K; Carey D E
SOURCE: AMERICAN JOURNAL OF DISEASES OF CHILDREN, (1986 Feb) 140 (2) 155-9.
Journal code: 0370471. ISSN: 0002-922X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198602
ENTRY DATE: Entered STN: 19900321
Last Updated on STN: 19900321
Entered Medline: 19860226

AB Russell-Silver syndrome (RSS) is a sporadic form of prenatal onset dwarfism with typical facial features, variable asymmetry, and linear growth 3 to 4 SDs below the mean. Endocrinologic studies are usually normal; however, six cases of RSS with ***growth*** ***hormone*** deficiency have been reported, three of which had additional pituitary abnormalities. We describe another case, a 7-year-old girl with RSS and deficiencies of ***growth*** ***hormone*** , corticotropin, and thyroid-stimulating hormone. ***Replacement*** ***therapy*** including ***growth*** ***hormone*** resulted in an improved growth velocity, though twice the usual ***dose*** of ***growth*** ***hormone*** was required and short stature persisted. Since ***growth*** ***hormone*** secretion is usually normal in RSS, the

existence of ***individuals*** with RSS phenotype and hypopituitarism including ***growth*** ***hormone*** deficiency suggests etiologic heterogeneity. We recommend that those ***individuals*** with RSS phenotype and a continuous significant decline in height velocity be investigated for pituitary abnormalities. Unusually high replacement ***doses*** of ***growth*** ***hormone*** may be required to overcome deficiency.

L16 ANSWER 15 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 2000:426393 BIOSIS
DOCUMENT NUMBER: PREV200000426393
TITLE: Similar response to ***growth*** ***hormone*** (GH) ***replacement*** ***therapy*** in men and women when the ***dose*** of GH is ***individualized*** .
AUTHOR(S): Koranyi, J. (1); Bengtsson, B.-A. (1); Johannsson, G. (1)
CORPORATE SOURCE: (1) Research Center for Endocrinology and Metabolism, Sahlgrenska University Hospital, Goteborg Sweden
SOURCE: Growth Hormone & IGF Research, (April, 2000) Vol. 10, No. Supplement B, pp. 134. print.
Meeting Info.: 28th International Symposium on GH and Growth Factors in Endocrinology and Metabolism Boston, Massachusetts, USA October 22-23, 1999
ISSN: 1096-6374.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L16 ANSWER 16 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2002346035 EMBASE
TITLE: Beneficial effects of growth hormone replacement in growth hormone-deficient adults.
AUTHOR: Blevins L.S.
CORPORATE SOURCE: Dr. L.S. Blevins, Vanderbilt Univ. School of Medicine, 2201 West End Avenue, Nashville, TN 37232, United States. lewis.Blevins@mcmail.vanderbilt.edu
SOURCE: Endocrinologist, (2002) 12/5 (405-411).
Refs: 54
ISSN: 1051-2144 CODEN: EDOCEB
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Adult ***growth*** ***hormone*** deficiency (AGHD) is associated with a reduction in lean body and muscle mass, an increased risk for cardiovascular morbidity and mortality, reduced muscle strength and impaired physical fitness, and decreased bone mass. These physical changes are often accompanied by impairment in psychological well-being. ***Growth*** ***hormone*** (GH) ***replacement*** ***therapy*** has proven to be beneficial in increasing lean body and muscle mass. Importantly, GH ***replacement*** ***therapy*** has significant positive effects on lipid profiles and central adiposity, two major cardiovascular risk factors. Improvements in bone mineral density are also often seen with ***replacement*** ***therapy*** . The diagnosis of AGHD should be considered in adults with a history of a mass lesion in the sella or hypothalamus, cranial irradiation, or documented childhood-onset GH deficiency. Adults with a history of head trauma should also be considered for this diagnosis. The traditional provocative test used for the diagnosis is the insulin tolerance test (ITT). However, the complexity and inherent risks associated with the ITT have resulted in many clinicians using arginine alone or in combination with GH-releasing hormone as the provocative test of choice. ***Growth*** ***hormone*** therapy should be ***individualized*** , with ***dose*** adjustments based on clinical and biochemical response. Serum insulin-like growth factor I concentrations are used to evaluate the effectiveness of therapy, with the goal of therapy to return these levels to the upper one-half of the normal age-adjusted and sex-adjusted normal ranges. Adverse effects of GH ***replacement*** ***therapy*** are minor and are minimized by ***individualizing*** therapy based on clinical response.

L16 ANSWER 17 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000049679 EMBASE
TITLE: Review of growth hormone therapy.
AUTHOR: Seligman T.M.
CORPORATE SOURCE: T.M. Seligman, Evergreen Integrative Medicine, 1821 NE 128 St., D. Kirkland, WA 98034, United States
SOURCE: Journal of Orthomolecular Medicine, (1999) 14/4 (219-226). Refs: 65
ISSN: 0317-0209 CODEN: JORMEI
COUNTRY: Canada
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
020 Gerontology and Geriatrics
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Hormone ***replacement*** ***therapy*** (HRT) is a well studied and accepted means of preventing disease and the symptoms associated with aging. In addition to a reduced production of the hormones estrogen, progesterone, dehydroepiandrosterone (DHEA), and testosterone, the production of ***growth*** ***hormone*** declines with age. Associated with the decline in these hormones is an increase in incidence of cardiovascular disease, osteoporosis and diabetes. In addition, an increased tendency towards central obesity and a decline in total muscle mass are associated with the aging process. New research is providing evidence of a protective effect of ***growth*** ***hormone*** replacement in aging ***individuals*** against the aforementioned diseases and body changes. Adverse effects of excess ***growth*** ***hormone*** have also been documented. These include an increased rate of proliferation of breast and prostate epithelial cells. Research is needed to determine the lowest possible ***dose*** of ***growth*** ***hormone*** that can be used to obtain benefit from this therapy and to limit the adverse effects.

L16 ANSWER 18 OF 19 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 96096867 EMBASE
DOCUMENT NUMBER: 1996096867
TITLE: [Alteration of carbohydrate metabolism induced by exogenous substances].
ALTERAZIONI DELL'EQUILIBRIO GLICOMETABOLICO INDOTTE DA SOSTANZA ESOGENE.
AUTHOR: Passera P.; Vitelli F.; Monaco A.; Porta M.; Molinatti G.M.
CORPORATE SOURCE: Istituto di Medicina Interna, Universita di Torino, Corso AM Dogliotti, 14,10126 Torino, Italy
SOURCE: Giornale Italiano di Diabetologia, (1995) 15/4 (327-340).
ISSN: 0391-7525 CODEN: GIDIDU
COUNTRY: Italy
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: Italian
SUMMARY LANGUAGE: Italian; English; Spanish
AB The hyperglycaemie effects of substances reported in the literature to be diabetogenic were systematically reviewed in this paper. Among anti-hypertensive drugs, thyazide diuretics induce ***dose*** -dependent insulin resistance. Non selective betablockers and clonidine slightly reduce insulin secretion, whereas diazoxyde is directly cytotoxic for beta-cells and its use has been advocated for the treatment of insulinomas. Early derivatives of nicotinic acid are the only hypolipaemic agents known to have a potentially diabetogenic effect. Among hormones, calcitonin administration causes transient reduction of insulin secretion, whereas factitious thyrotoxycosis may induce more severe hyperglycaemia. Abnormally high prevalence of impaired glucose tolerance (IGT) has been reported among 'body-builders' taking anabolic steroids. Low-progesterone oral contraceptives do not interfere with carbohydrate metabolism, nor does ***replacement*** ***therapy*** with ***growth*** ***hormone*** in hyposomatism. Catecholamines are only utilized in emergencies, so that their diabetogenic potential hardly ever becomes clinically evident. Administration of L-DOPA may induce mild hyperinsulinaemia, whilst opioids stimulate glucagon secretion which may

impair glucose tolerance, as observed among illicit drug users. Some substances used in neurology and psychiatry may produce various diabetogenic effects through different mechanisms: high- ***dose*** diphenylhydantoin inhibits insulin secretion, phenothiazines, benzodiazepines and tricyclic antidepressants may unmask latent IGT in predisposed ***individuals*** , because of the sympathetic activation evoked through their hypotensive effect. Among non steroid anti-inflammatory drugs, only indomethacin may be indirectly diabetogenic because of its inhibition of PGE catabolism. More relevant from a clinical point of view, antimitotic agents may be betacytotoxic (alloxan, streptozotocin), inhibit insulin synthesis (Lasparaginase), or be diabetogenic through unknown mechanisms in men (cyclophosphamide) and animals (vincristine). Immunomodulators used after organ transplant or in the treatment of chronic liver disease have sometimes exhibited betacytotoxicity (high- ***dose*** cyclosporin), insulin resistance (FK506), or multiple diabetogenic mechanisms) alphainterferon). Didanosin, a hepatotoxic antiviral agent, is also diabetogenic. Overall, data in the literature suggest that few substances are endowed with a clinically important diabetogenic effect, and that this is only manifested in predisposed ***individuals*** .

L16 ANSWER 19 OF 19 SCISEARCH COPYRIGHT 2002 ISI (R)
ACCESSION NUMBER: 1999:209232 SCISEARCH
THE GENUINE ARTICLE: 174JT
TITLE: Effect of growth hormone (GH) during puberty in GH-deficient children: preliminary results from an ongoing randomized trial with different dose regimens
AUTHOR: Wikland K A (Reprint); Alm F; Aronsson S; Gustafsson J; Hagenas L; Hager A; Ivarsson S; Kristrom B; Marcus C; Moell C; Nilsson K O; Ritzen M; Tuvemo T; Westgren U; Westphal O; Aman J
CORPORATE SOURCE: UNIV GOTHENBURG, DEPT PEDIAT, INT PEDIAT GROWTH RES CTR, SAHLGRENSKA UNIV HOSP E, SE-41685 GOTHENBURG, SWEDEN (Reprint); KAROLINSKA INST, STOCKHOLM, SWEDEN; HALMSTAD CTY HOSP, HALMSTAD, SWEDEN; UPPSALA ACAD HOSP, UPPSALA, SWEDEN; LINKOPING HOSP, LINKOPING, SWEDEN; MALMO GEN HOSP, S-21401 MALMO, SWEDEN; UMEA REG HOSP, UMEA, SWEDEN; HUDDINGE HOSP, S-14186 HUDDINGE, SWEDEN; LUND HOSP, LUND, SWEDEN; OREBRO MED CTR HOSP, S-70185 OREBRO, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: ACTA PAEDIATRICA, (FEB 1999) Vol. 88, Supp. [428], pp. 80-84.
Publisher: SCANDINAVIAN UNIVERSITY PRESS, PO BOX 2959 TOYEN, JOURNAL DIVISION CUSTOMER SERVICE, N-0608 OSLO, NORWAY.
ISSN: 0803-5253.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 20
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This paper reports results from an ongoing. randomized, multicentre national trial. The aim is to elucidate whether a ***dose*** of ***growth*** ***hormone*** (GH) of 0.2 IU/kg (0.07 mg/kg), given either as once-daily or twice-daily injections during puberty, is more effective than a once-daily ***dose*** of 0.1 IU/kg/day (0.03 mg/kg/day) in improving final height in children with GH deficiency (GI ID). The twice-daily regimen comes closer to the spontaneous GI-1 secretion pattern in puberty, Ninety-two children with GHD who had been receiving GH therapy fur at least 1 year, and with spontaneous puberty or who were prepubertal and due to be started on ***replacement*** ***therapy*** to induce puberty, were randomly assigned to receive GH as follows: group A, 0.1 IU/kg/day (0.03 mg/kg/day, administered once daily; group B, 0.2 IU/kg/day (0.07 mg/kg/day), administered once daily; and group C, 0.2 IU/kg/day (0.07 mg/kg/day), divided into two equal injections given at 12-hour intervals. Pubertal height gain was 0.7, 0.7 and 1.3 SDS fur groups A, B and C, respectively. The gain in height during puberty was thus most marked in group C. Mean final height, when corrected for parental height. was between 0 and 1 SDS in all treatment groups. All but seven children reached a final height within +/- 2 SD of the general population. There was a wide range of final heights in all three treatment groups. This variation in response suggests the need to

individualize treatment in order to achieve an appropriate final height for most ***individuals*** .

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=> d his

     (FILE 'HOME' ENTERED AT 15:19:58 ON 29 NOV 2002)

     FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     15:20:28 ON 29 NOV 2002
L1        209152 S GROWTH HORMONE
L2             2 S REPLCEMENT THERAPY
L3         73580 S REPLACEMENT THERAPY
L4             0 S L1 (P) L2
L5          2712 S L1 (P) L3
L6         13208 S (INITIAL DOSE)
L7          9172 S (MAINTENANCE DOSE)
L8             0 S L5 (P) L6 (P) L7
L9         77643 S MICROSPHERE
L10            0 S L5 (P) L9
L11          215 S L5 (P) INDIVIDUAL?
L12           66 S L11 (P) DOSE
L13           27 S L5 (P) (L6 OR L7)
L14           10 DUPLICATE REMOVE L13 (17 DUPLICATES REMOVED)
L15           24 DUPLICATE REMOVE L12 (42 DUPLICATES REMOVED)
L16           19 S L15 NOT L14

=> log y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                51.77      51.98

STN INTERNATIONAL LOGOFF AT 15:26:43 ON 29 NOV 2002
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